Section I
Amendments to the Specification

Please insert the following replacement title at page 1, lines 1-2:

Cytotoxic cyplasin of the sea hare, ~~Aplysia punctata~~ *Aplysia punctata*, cDNA cloning and expression of bioreactive recombinants

Please insert the following replacement paragraph at page 3, line 30:

~~Figure legends~~BRIEF DESCRIPTION OF THE DRAWINGS

Please insert the following replacement paragraph at page 4, lines 7-9 (added material indicated by double underlining pursuant to instructions from Gina Jones of the "Amendment Practice" section of the USPTO; single underlining is intended to be present in text after entry of amendment):

(a) Amino acid sequences of precursor proteins derived from A. punctata cDNAs comprising the nucleotide sub-sequences coding for the (underscored) internal peptide SGDYILIASYAD (SEQ ID NO: 4)

Please insert the following replacement paragraphs at page 4, lines 10-27

The upper sequence (SEQ ID NO: 1; 558 aa residues) is derived from the nucleotide sequence of the cDNA encoding the polypeptide termed cyplasin-L, and the-lower sequence (SEQ ID NO: 2; 421 aa residues) is derived from the nucleotide sequence of the cDNA encoding the polypeptide termed cyplasin-S. The nucleotide sequences are found in databases under the accession numbers AJ304802 (cyplasin-L cDNA) and AJ304801 (cyplasin-S cDNA). In addition to these clearly distinguishable transcripts other mRNAs may exist with additional differences. PCR with total cDNA as template and cyplasin-L specific primer pairs releases sequences slightly differing from the cloned cyplasin-L and cyplasin-S encoding cDNA sequences. Amino acid exchanges detected by the PCR procedure are indicated in brackets. Asn-linked glycosylation sites are found at aa positions N-151, N-271, N-401, N-416 and N-.422. The putative cleavage point of the secretory signal sequence is between aa 52 (S) and aa 53 (A).

(b) Nucleotide sequence of the protein Cypl-Mut-(-Sig.Seq) (SEQ ID NO: 5)

Please insert the following replacement paragraph at page 5, lines 2-24:

Extracts containing the cytotoxic factor were prepared from SF9 cells expressing cyplasin-L-EGFP as described under materials and methods. Identical samples were separated on a 12% polyacrylamide gel. Polypeptides run on parallel gel sections together with a protein size marker were either visualized by a silver-staining procedure or blotted to a PVDF membrane. The membrane was probed with an anti-EGFP antibody and immuno-complexes formed were visualized by means of an alkaline phosphatase-coupled second antibody. ~~(a)~~ The left lane of the gel in FIG. 4 shows the protein size marker. ~~(b)~~ The middle lane of the gel in FIG. 4 shows the prominent polypeptides present in the extract, ~~(c)~~ and the right lane of the gel in FIG. 4 shows the antigen detected by the EGFP-specific antibody. It should be noted that the anti-EGFP antibody detects a polypeptide in the order of 70 kDa which is significantly larger than EGFP (27 kDa). This result indicates the enrichment of the EGFP-tagged fusion protein in the cytotoxic fraction. The calculated molecular mass of the fusion protein between the cyplasin-L precursor protein (57.2 kDa) and EGFP is 84.2 kDa. The processed cyplasin-L with deleted signal sequence has a calculated molecular mass of 41.6 kDa resulting in a molecular mass of 68.6 kDa when fused to EGFP which is close to the size of the fusion protein detected on the blot. Accordingly, it has to be assumed that the cytotoxic extract contains the EGFP-tagged and processed cyplasin-L.

Please insert the following replacement paragraph at page 7, lines 18-20:

The highest probability for cleavage was determined to be between aa positions 19 and 20 of SEQ ID NO: 1 or 2 or (with lower probability) between aa positions 52 and 53 of SEQ ID NO: 1 or 2.

Please insert the following replacement paragraph at page 21, lines 18-33:

(F) Molecular Cloning of cDNAs Encoding Proteins Comprising the Peptide SGDYILIASYAD (SEQ ID NO: 4)

Amplified cDNA was used as a template and PCR reactions were primed with combinations of specific primers corresponding to the search sequence and with non-specific primers, e.g. modified oligo-dT and Smart II, respectively. Amplification products were recloned in a pBluescript-derived T-overhang vector and sequenced. The validity of these sequences was

verified by PCR reactions primed with oligo deoxynucleotides corresponding to sequences upstream and downstream of the specific SGDYILIASYAD-encoding primer. These probe-independent products contained the nucleotide sequence encoding the peptide SGDYILIASYAD (SEQ ID NO: 4). Sequences found upstream of SGDYILIASYAD-encoding sequence were unique, except for several base exchanges discussed in the text. In contrast, two 3' end sequences could be detected differing in length (L and S).

Please insert the following replacement paragraph at pages 25, line 29 to page 26, line 14:

cDNA prepared from RNA of the albumen gland of *A. punctata* comprises more than one transcript encoding the peptide SGDYILIASYAD (SEQ ID NO: 4). Two cDNAs were cloned encoding proteins which diverge significantly in their carboxy-terminal sections but which comprise the target sequence (FIG. 2). One of these cDNAs encodes a protein of 558 aa residues with a molecular mass of 62.4 kDa (termed cyplasin-L; SEQ ID NO: 1) while another cDNA reflects a transcript encoding a shorter protein (421 aa residues, molecular mass 46.9 kDa, termed cyplasin-S; SEQ ID NO: 2). Moreover, PCR on total cDNA with cyplasin-L specific primer pairs results in DNA fragments whose sequences diverge from those encoding cyplasin-L and cyplasin-S, respectively. Accordingly, mRNAs appear to exist which are neither identical with cyplasin-L nor with cyplasin-S. These sequence micro heterogeneities suggest that *A. punctata* produces an unknown number of very similar but not 100% identical proteins that comprise the target sequence. On the basis of the available data it cannot be decided whether these different mRNAs and proteins derive from one single gene, e.g. by alternative splicing in combination with RNA editing, or whether there exists a cluster of very similar but not 100% identical genes.